ABSTRACT OF THE DISCLOSURE

Microarrays can measure the expression of thousands of genes and thus identify changes in expression between different biological states. Methods are needed to determine the significance of these changes, while accounting for the enormous number of genes. We describe a new method, Significance Analysis of Microarrays (SAM), that assigns a score to each gene based on the change in gene expression relative to the standard deviation of repeated measurements. For genes with scores greater than an adjustable threshold, SAM uses permutations of the repeated measurements to estimate the percentage of such genes identified by chance, the false discovery rate (FDR). When the transcriptional response of human cells to ionizing radiation was measured by microarrays, SAM identified 34 genes that changed at least 1.5-fold with an estimated FDR of 12%, compared to FDRs of 60% and 84% using conventional methods of analysis. Of the 34 genes, 19 were involved in cell cycle regulation, and 3 in apoptosis. Surprisingly, 4 nucleotide excision repair genes were induced, suggesting that this repair pathway for UV-damaged DNA might play a heretofore unrecognized role in repairing DNA damaged by ionizing radiation.